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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,877	02/02/2005	Takehiko Nomura	0020-5340PUS1	5247

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
MACAULEY, SHERIDAN R	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
08/10/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/522,877	NOMURA ET AL.	
	Examiner	Art Unit	
	Sheridan R. MacAuley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11,14-22 and 24-41* is/are pending in the application.

4a) Of the above claim(s) *7-10,20-22,24-36 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,11,14-19, 37-39 and 41* is/are rejected.

7)☒ Claim(s) *6, 18 and 38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/02/2005, 02/02/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 4-11, 14-22 and 24-41 are pending.

Election/Restrictions

1. Applicant's election of claims 1, 2, 4-6, 11, 14-19, 37-39 and 41 in the reply filed on May 30, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is therefore made FINAL.

2. Claims 7-10, 20-22, 24-36 and 40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

3. Claims 1, 2, 4-6, 11, 14-19, 37-39 and 41 are examined on the merits in this office action

Information Disclosure Statement

4. The information disclosure statements filed on February 2, 2005 and June 2, 2005 fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be

listed. Specifically, copies were not provided for those references that are struck through on the IDS, and the information in the references has not been considered.

Specification

5. The use of trademarks, such as TWEEN 80, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Objections

6. Claims 6, 18 and 38 objected to because of the following informalities. It is recommended that the claims be amended as follows: In claim 6, the term BCG-CWS should be preceded by the full term, and the abbreviation should be placed in parentheses. In claim 18, the term TWEEN 80 should be capitalized. In claim 38, the word "exhibit" should be changed to "exhibits". Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "(25°C)" in the claims renders the claims indefinite because it is unclear whether or not it is a required limitation of the claim. If the term is a required limitation of the claim, it is recommended that the claims be amended to recite "poise at 25°C".

9. Claims 2, 4-6, 14-19, 37-39 and 41 are rejected insofar as they depend from claim 1.

10. Claim 15 is also rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear whether applicant intends for the composition to comprise 0.66 g to 3.35 g of the bacterial CWS wherein 0.4 to 8 weight% of the oil per 2 liters of water have been added (i.e. 0.66 g to 3.35 g of the bacterial CWS with an aqueous solution comprising 0.02 to 0.4 weight% of the oil), or an aqueous solution comprising 0.66 g to 3.35 g of the bacterial CWS per 2 liters of water, and 0.4 to 8 weight% of the oil per 2 liters of water.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 2, 4-6, 11, 14-19, 37, 39 and 41 are rejected under 35 U.S.C. 102(b) as anticipated by Azuma et al. (EP 1097715 A1, cited in prior action). Claim 1 recites a paste comprising bacterial cell wall skeleton components (bacteria-CWS) and an oil wherein the paste has a viscosity of 0.7 poise or less (25 degrees C). Claim 2 recites the paste comprising bacteria-CWS according to claim 1 wherein the paste has a viscosity between 0.2 and 0.7 poise at 25.degree. C. Claim 4 recites the paste comprising bacteria-CWS according to claim 1 wherein the bacteria-CWS is BCG-CWS. Claim 5 recites the paste comprising bacteria-CWS according to claim 1, wherein the oil is squalane. Claim 6 recites the paste according to claim 1, wherein the bacteria-CWS is BCG-CWS and wherein the paste comprises 6.6 g to 35.2 g of squalane per about 0.67 g of BCG-CWS. Claim 11 recites the paste comprising bacteria-CWS obtained by the process for preparation according to claim 7. Claim 14 recites the paste according to claim 1 that is formulated as an oil-in-water emulsion and further comprises a surfactant, a stabilizer, and water. Claim 15 recites the paste according to claim 14, which comprises 0.66 g to 3.35 g of the bacteria-CWS, and 0.4 wt % to 8 wt % of the oil per 2 liters of water. Claim 16 recites the paste according to claim 14, wherein the stabilizer comprises 1 to 10% mannitol. Claim 17 recites the paste according to claim 14, wherein the surfactant comprises 0.01% to 3% polyethyleneoxysorbitan fatty acid ester. Claim 18 recites the paste according to claim 17, wherein the polyethyleneoxysorbitan fatty acid ester is TWEEN 80. Claim 19 recites the paste

according to claim 14, having the following properties: (1) the particle diameter of an oil droplet of the emulsion is 0.2 to 30 micron; (2) the bacteria-CWS is encapsulated in the oil droplet, and is negative for reaction with lectin. Claim 37 recites the paste of claim 1 that is formulated as an assembly of bacteria-CWS particles wherein the particle diameter is from 0.1 micron to 20 micron in the particle size distribution. Claim 38 recites the paste according to claim 37, wherein the assembly of bacteria-CWS particles exhibits a particle size distribution showing a single peak as well as D10%: 0.23 ± 0.05 microns and D90%: 0.60 ± 0.05 microns. Claim 39 recites the paste according to clam 37 that is formulated as an oil-in-water emulsion that further comprises a surfactant, a stabilizer, and water. Claim 41 recites a pharmaceutical composition comprising the emulsion according to claim 14.

13. Azuma teaches a paste comprising bacterial CWS (including BCG-CWS, i.e. CWS from the BCG strain of *Mycobacterium bovis*) and an oil (squalane). Azuma teaches that the composition may comprise a surfactant (0.2% TWEEN 80, i.e. polysorbate 80), a stabilizer (2.3% mannitol) and water (p. 10, table 1). Azuma teaches that the particle diameter of the droplets is from 0.1 to 20 microns, that the bacterial CWS is encapsulated in the oil droplet and is negative for a reaction with lectin (p. 3, lines 10-18, p. 4, lines 6-14 and p. 6, lines 13-17). Azuma teaches that the paste is formulated as an assembly of bacterial CWS particles, and as an oil-in-water emulsion (p. 4, lines 4-22). Azuma et al. teaches that the emulsion can be used as a pharmaceutical composition (p. 8, lines 51-53). Azuma teaches a composition comprising about 21.4 g squalane per 0.67 g BCG-CWS (i.e. 32 g squalane per 1 g

BCG-CWS, which falls within the range recited in claim 6; 6.6 g to 35.2 g squalane per 0.67 g BCG-CWS; p. 10, lines 1-8). Azuma teaches a composition comprising 1 g of bacterial CWS and about 1.6 weight% of oil per 2 liters of water (i.e. 32 g squalane in 2000 ml of aqueous solution; p. 10, lines 1-8).

14. Moreover, the claimed characteristic (i.e. viscosity of 0.7 poise or less, specifically between 0.2 and 0.7 poise) must be inherent to the reference composition. The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new. Thus the claiming of a new use, functions or unknown property that is inherently present in the prior art does not necessarily make the claim patentable. See MPEP 2112.

15. Therefore, Azuma teaches all of the limitations of the cited claims, or, in the alternate, the cited claims are rendered obvious over the teachings of Azuma.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1, 2, 4-6, 11, 14-19, 37-39 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Azuma (EP 1097715 A1, cited in prior action) in view of Van Nest et al. (EP 0399843 A2). Claim 1 recites a paste comprising bacterial cell wall skeleton components (bacteria-CWS) and an oil wherein the paste has a viscosity of 0.7 poise or less (25 degrees C). Claim 2 recites the paste comprising bacteria-CWS according to claim 1 wherein the paste has a viscosity between 0.2 and 0.7 poise at 25.degree. C. Claim 4 recites the paste comprising bacteria-CWS according to claim 1 wherein the bacteria-CWS is BCG-CWS. Claim 5 recites the paste comprising bacteria-

CWS according to claim 1, wherein the oil is squalane. Claim 6 recites the paste according to claim 1, wherein the bacteria-CWS is BCG-CWS and wherein the paste comprises 6.6 g to 35.2 g of squalane per about 0.67 g of BCG-CWS. Claim 11 recites the paste comprising bacteria-CWS obtained by the process for preparation according to claim 7.. Claim 14 recites the paste according to claim 1 that is formulated as an oil-in-water emulsion and further comprises a surfactant, a stabilizer, and water. Claim 15 recites the paste according to claim 14, which comprises 0.66 g to 3.35 g of the bacteria-CWS, and 0.4 wt % to 8 wt % of the oil per 2 liters of water. Claim 16 recites the paste according to claim 14, wherein the stabilizer comprises 1 to 10% mannitol. Claim 17 recites the paste according to claim 14, wherein the surfactant comprises 0.01% to 3% polyethyleneoxysorbitan fatty acid ester. Claim 18 recites the paste according to claim 17, wherein the polyethyleneoxysorbitan fatty acid ester is Tween 80. Claim 19 recites the paste according to claim 14, having the following properties: (1) the particle diameter of an oil droplet of the emulsion is 0.2 to 30 micron; (2) the bacteria-CWS is encapsulated in the oil droplet, and is negative for reaction with lectin. Claim 37 recites the paste of claim 1 that is formulated as an assembly of bacteria-CWS particles wherein the particle diameter is from 0.1 micron to 20 micron in the particle size distribution. Claim 38 recites the paste according to claim 37, wherein the assembly of bacteria-CWS particles exhibits a particle size distribution showing a single peak as well as D10%: 0.23 ± 0.05 microns and D90%: 0.60 ± 0.05 microns. Claim 39 recites the paste according to clam 37 that is formulated as an oil-in-water emulsion that further

comprises a surfactant, a stabilizer, and water. Claim 41 recites a pharmaceutical composition comprising the emulsion according to claim 14.

20. Azuma teaches a paste comprising bacterial CWS (including BCG-CWS, i.e. CWS from the BCG strain of *Mycobacterium bovis*) and an oil (squalane). Although Azuma does not disclose the viscosity of the paste, it is made by nearly identical methods to those described in the instant application (p. 17, line 57-p. 18, line 5). The paste of Azuma would therefore inherently have a viscosity within the disclosed range. Azuma teaches that the composition may comprise a surfactant (0.2% TWEEN 80, i.e. polysorbate 80), a stabilizer (2.3% mannitol) and water (p. 10, table 1). Azuma teaches that the particle diameter of the droplets is from 0.1 to 20 microns, that the bacterial CWS is encapsulated in the oil droplet and is negative for a reaction with lectin (p. 3, lines 10-18, p. 4, lines 6-14 and p. 6, lines 13-17). Azuma teaches that the paste is formulated as an assembly of bacterial CWS particles, and that the paste is formulated as an oil-in-water emulsion (p. 4, lines 4-22). Azuma et al. teaches that the emulsion can be used as a pharmaceutical composition (p. 8, lines 51-53). Azuma teaches a composition comprising about 21.4 g squalane per 0.67 g BCG-CWS (i.e. 32 g squalane per 1 g BCG-CWS, which falls within the range recited in claim 6, 6.6 g to 35.2 g squalane per 0.67 g BCG-CWS; p. 10, lines 1-8). Azuma teaches a composition comprising 1 g of bacterial CWS and about 1.6 weight% of oil per 2 liters of water (i.e. 32 g squalane in 2000 ml of aqueous solution; p. 10, lines 1-8). Azuma also teaches that a composition with a single peak for particle size is preferable because it is indicative of stability of the composition (p. 6, lines 18-23).

21. Azuma does not specifically teach a composition wherein the particle size distribution shows a single peak as well as D10%: 0.23 ± 0.05 microns and D90%: 0.60 ± 0.05 microns.

22. Van Nest teaches a composition which is an oil-in-water emulsion comprising a muramyl dipeptide derivative (MTP-PE, see p. 2, lines 41-55) and an oil, wherein the particle size is less than one micron, specifically between 0.5 and 0.8 microns (p. 24, lines 25-42). Van Nest teaches that reducing oil droplet size improves the adjuvant performance (p. 24, lines 41-42). Van Nest teaches a method of reducing oil droplet size in the composition (p. 7, lines 12-22).

23. At the time of the invention, a composition comprising nearly all of the claimed elements was known, as taught by Azuma. Although Azuma does not disclose the viscosity of the paste, it is made by nearly identical methods to those described in the instant application (p. 17, line 57-p. 18, line 5). The paste of Azuma would therefore be expected to have a viscosity within the disclosed range. It was also known at the time of the invention that the particle size of oil-in-water compositions comprising similar components could be reduced within the claimed range, and that compositions comprising a single peak for particle size distribution are preferential, as taught by Van Nest and Azuma, respectively. One of ordinary skill in the art would have been motivated to reduce the particle size of the oil-in-water emulsion of Azuma to the range taught by Van Nest because Van Nest teaches that the reduced droplet size improves the performance of the compound as an adjuvant. One would have a reasonable expectation of success in reducing droplet size because methods to reduce droplet size

were successfully employed by Van Nest using a similar composition. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

24. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan R. MacAuley whose telephone number is (571) 270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM

/Ruth A Davis/
Primary Examiner, AU 1651